

[0035] FIG. 5 shows a graph of the acid-base surface energy profiles for particles formed in second liquids of varying polarity and acid-base properties.

[0036] FIG. 6 shows a graph of the X-ray diffraction profiles for solid proteinaceous matter from a common first liquid compared to standard lyophilization matter.

[0037] FIGS. 7A-7C show images of human IgG particles formed through methods of the disclosure at different voltages.

[0038] FIG. 8 shows a graph of volume-weighted size distributions for human IgG particles D10, D50, and D90, formed through methods of the disclosure at different voltages.

[0039] FIG. 9 shows a graph of a relationship between particle mass and environmental humidity for particles formed through methods of the disclosure at fixed temperature.

[0040] FIG. 10 shows a graph of a differential scanning calorimetry measurement used to measure the glass transition temperature for particles formed through methods of the disclosure.

[0041] FIG. 11 shows a graph of the percentages of dissolved particles after storage for several suspensions of human IgG particles that were suspended in aqueous solutions comprising various crowding agents.

[0042] FIG. 12 shows pictures of the sedimentation and surface adhesion properties of human IgG particles that are suspended in a non-aqueous suspension medium.

[0043] FIG. 13 shows a graph of the surface tension of the air-liquid interface for a neat deionized water solution and a solution of protein dissolved in deionized water at a concentration of 20 mg/mL.

[0044] FIG. 14A shows an image of a human IgG particle surface formed through methods of the disclosure.

[0045] FIG. 14B shows an image of a human IgG particle sectioned to reveal the internal cross-section.

DETAILED DESCRIPTION

[0046] Particles have been produced using various techniques. For example, the generation of particles can be accomplished by producing a droplet of a liquid comprising an active agent dissolved in a solvent. The solvent can then be extracted from the droplets by depositing the droplets into a liquid in which the solvent, but not the active agent, is soluble leaving behind a solid particle. Isolation of the particles occur following evaporation of the liquids. However, the application of these techniques to form functional circular particles have been limited due to the lack of sufficient control over size uniformity, shape selectivity, surface functionality and skeletal density of the particles which are often difficult to obtain. The present disclosure seeks to mitigate the control issues that are associated with forming functional particles by providing a robust and controlled method for particle preparation.

[0047] The present disclosure generally relates to a particle comprising an agent or a composition comprising a plurality of particles comprising an agent suspended in a liquid, wherein the particle or the plurality of particles comprises less than about 25% internal void spaces and the circularity of the particle is from about 0.10 to about 1.00.

[0048] The present disclosure also relates to methods of forming particles, the method comprising: a) providing droplets comprising a first liquid and an agent; b) contacting the droplets with a second liquid; c) allowing the droplets to

dry; and d) removing the first and second liquids, thereby forming particles comprising an agent, wherein the particles comprise less than about 25% internal void spaces and the circularity of the particles is from about 0.10 to about 1.00 after removing the first and second liquids.

[0049] In certain aspects, the disclosure generally relates to a method of controlling the morphology of particles, the method comprising: a) providing droplets comprising a first liquid and an agent; b) contacting the droplets with a second liquid under a specified Peclet number; c) allowing the droplets to dry; and d) removing the first and second liquids, wherein the specified Peclet number controls the morphology of the particles.

[0050] In certain other aspects, the disclosure generally relates to a method of controlling the surface properties of particles, the method comprising: a) providing droplets comprising a first liquid, a first component, and a second component, wherein the first component is present in an amount closer to its solubility limit than the second component, the first component has a higher Peclet number than the second component, or a combination thereof; b) contacting the droplets with a second liquid; c) allowing the droplets to dry; and d) removing the first and second liquids, thereby forming particles, wherein the first component is enriched at the surface of the particles relative to the second component.

[0051] As described herein, the disclosure provides methods for the preparation of particles including one or more agents, e.g., therapeutic or diagnostic agents. The particles can be formed by creating droplets of a first liquid, e.g., including an agent, and removing the first liquid, e.g., through its dispersal in a second liquid and/or evaporation, to solidify the droplets. The process of forming the particles as described herein, significantly alters the structure or morphology of the particles and may enhance the stability of the agents. For example, the particles may be stored for extended periods of time without significant loss of activity or the need for refrigeration. These particles may be used to generate stabilized pharmaceutical compositions, pharmaceutical suspension formulations, pharmaceutical powder formulations (e.g., inhalable powders, injectable powders), creams or other topical pastes, nutraceuticals, or cosmetics. The term “pharmaceutical composition” as used herein, denotes a composition in which a therapeutic or diagnostic agent retains, or partially retains, its intended biological activity or functional form, and in which only pharmaceutically acceptable components are included.

[0052] It will be readily understood that the aspects and embodiments, as generally described herein, are exemplary. The following more detailed description of various aspects and embodiments are not intended to limit the scope of the present disclosure, but is merely representative of various aspects and embodiments. Moreover, the compositions and methods disclosed herein may be changed by those skilled in the art without departing from the scope of the present disclosure. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which this disclosure belongs. All publications and patents referred to herein are incorporated by reference.